

Substitute for form 1449A/PTO

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

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Sheet 1 of 7

Complete if Known

Application Number	
Filing Date	On Even Date Herewith
First Named Inventor	Paz EINAT
Group Art Unit	1635
Examiner Name	
Attorney Docket Number	EINAT=1.1D

JC986 U.S. PRO  
10/09/1333  
03/06/02

U.S. PATENT DOCUMENTS						
Examiner Initials*	Cite No. <sup>1</sup>	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number	Kind Code <sup>2</sup> (if known)			
1822	AA	3,791,993		Schuurs et al	02-12-1974	
	AB	3,838,153		Schuurs et al	10-01-1974	
	AC	3,850,578		McConnell	11-26-1974	
	AD	3,850,572		Schuurs et al	11-26-1974	
	AE	3,853,987		Dreyer	12-10-1974	
	AF	3,867,517		Ling	02-17-1975	
	AG	3,879,262		Schuurs et al	04-22-1975	
	AH	3,901,654		Gross	08-26-1975	
	AI	3,935,074		Rubenstein et al	01-27-1976	
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	AL	4,034,074		Miles	07-04-1977	
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	AP	4,736,866		Leder et al	04-12-1988	
	AQ	4,801,531		Frossard	01-31-1989	
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	AS	4,873,191		Wagner et al	10-10-1989	
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	AU	5,011,771		Bellet et al	04-30-1991	
	AV	5,175,383		Leder et al	12-29-1992	
	AW	5,175,384		Krimpenfort et al	12-29-1992	
22	AX	5,175,385		Wagner et al	12-29-1992	
	AY	5,192,659		Simons	03-09-1993	
	AZ	5,221,778		Byrne et al	06-22-1993	
	BA	5,225,347		Goldberg et al	07-06-1993	
	BB	5,272,057		Smulson	12-21-1993	
	BC	5,281,521		Trojanowski et al	01-25-1994	
	BD	5,288,846		Quertermous et al	02-22-1994	
	BE	5,298,422		Schwartz et al	03-29-1994	
22	BF	5,347,075		Sorge	09-13-1994	
	BG	5,360,735		Weinshank et al	11-01-1994	
	BH	5,387,742		Cordell	02-07-1995	
	BI	5,464,764		Capecchi et al	11-07-1995	
	BJ	5,487,992		Capecchi et al	01-30-1996	
22	BK	5,614,396		Bradley et al	03-25-1997	

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<sup>1</sup> Unique citation designation number. <sup>2</sup> See attached Kinds of U.S. Patent Documents. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. <sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.

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Sheet 2 of 7

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## **FOREIGN PATENT DOCUMENTS**

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		Office <sup>3</sup>	Number					
	BL	WO	93/1420			07-22-1993		
	BM	WO	94/06908			03-31-1994		
	BN	WO	94/23649			10-13-1994		
	BO	WO	94/28123			12-08-1994		

## **OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS**

Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T <sup>2</sup>
	BP	Agrawal S, "Antisense oligonucleotides: towards clinical trials", <u>Trends Biotechnol.</u> 14(10):376-387 (1996)	
	BQ	Akhter et al, "Interactions of antisense DNA oligonucleotide analogs with phospholipid membranes (liposomes)", <u>Nuc. Res.</u> 19:5551-5559 (1991)	
	BR	Alon et al, "Vascular endothelial growth factor acts as a survival factor for newly formed retinal vessels and has implications for retinopathy of prematurity", <u>Nat. Med.</u> 1(10):1024-1028 (1995)	
	BS	ATTWOOD, T, "The Bable of Bioinformatics", <u>Science</u> 290:471-473 (2000)	
	BT	Benjamin et al, "Conditional switching of vascular endothelial growth factor (VEGF) expression in tumors: induction of endothelial cell shedding and regression of hemangioblastoma-like vessels by VEGF withdrawal", <u>Proc. Natl. Acad. Sci. USA</u> 94(16):8761-8766 (1997).	
	BU	BERENDSEN, H, "A Glimpse of the Holy Grail?", <u>Science</u> 282:642-643 (1998)	
	BV	Blaesse, "Gene Therapy for Cancer", <u>Sci. Am.</u> 276(6):111-115 (1997)	
	BW	Bouck et al, "How tumors become angiogenic" <u>Adv. Cancer Res.</u> 69:135-174 (1996)	
	BX	Bunn et al, "Oxygen sensing and molecular adaptation in hypoxia", <u>Physiol. Rev.</u> 76:839-885 (1996)	

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Sheet 3

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First Named Inventor

Paz EINAT

Group Art Unit


1635

Examiner Name

Attorney Docket Number

EINAT=1.1D

BY	Burke et al, "Preparation of Clone Libraries in Yeast Artificial-Chromosome Vectors", in <u>Methods in Enzymology</u> , Vol 194, "Guide to Yeast Genetics and Molecular Biology", eds. Guthrie et al, Academic Press, Inc. Chap. 17, pp. 251-270 (1991)
BZ	Calabretta et al, "Antisense strategies in the treatment of leukemias", <u>Semin. Oncol.</u> 23:78 (1996)
CA	Capecchi, "Altering the genome by homologous recombination", <u>Science</u> 244:1288-1292 (1989)
CB	Carmeliet et al, "Role of HIF-1alpha in hypoxia-mediated apoptosis, cell proliferation and tumour angiogenesis", <u>Nature</u> 394(66923): 485-490 (1998)
CC	Crooke, "Progress in antisense therapeutics", <u>Hematol. Pathol.</u> 2:59 (1995)
CD	Davies et al, "Targeted alterations in yeast artificial chromosomes for inter-species gene transfer", <u>Nucleic Acids Research</u> 20(11):2693-2698 (1992)
CE	de Gruyter, <u>Concise Encyclopedia Biology</u> , p. 32
CF	Dickinson et al, "High frequency gene targeting using insertional vectors", <u>Human Molecular Genetics</u> 2(8):1299-1302 (1993)
CG	Duff et al, "Insertion of a pathogenic mutation into a yeast artificial chromosome containing the human APP gene and expression in ES cells", <u>Research Advances in Alzheimer's Disease and Related Disorders</u> (1995)
CH	Duke et al, "Cell Suicide in Health and Disease", <u>Sci. Am.</u> , pp. 80-87 (1996)
CI	Eckstein, "Nucleotide Phosphorothioates", <u>Ann. Rev. Biochem.</u> 54:367-402 (1985)
CJ	Felgner, "Nonviral Strategies for Gene Therapy", <u>Sci. Am.</u> , pp. 102-106 (1997)
CK	Fyodorov et al, et-1, a novel ETS domain factor that can activate neuronal nAChR gene transcription", <u>J. Neurobiol.</u> 34(2):151-163 (1998)
CL	Gallagher et al, "Identification of p53 Genetic Suppressor Elements which Confer Resistance to Cisplatin", <u>Oncogene</u> 14:185-193 (1997)

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Sheet

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Attorney Docket Number

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**OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS**

Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T <sup>2</sup>
	CM	GALPERIN et al, "Who's your neighbor? New computational approaches for functional genomics", <u>Nature Biotechnol</u> 18:609-613 (2000)	
	CN	Gewritz, "Oligodeoxynucleotide-based therapeutics for human leukemias", <u>Stem Cells Dayt</u> , 11:96 (1993)	
	CO	Gordon, Transgenic Animals", <u>Intl. Rev. Cytol</u> , 115:171-229 (1989)	
	CP	Hanahan et al, "Patterns and Emerging Mechanisms of Angiogenic Switch During Tumorigenesis" <u>Cell</u> 86:353-364 (1996)	
	CQ	Hanania et al, "Recent advances in the application of gene therapy to human disease", <u>Am. J. Med.</u> 99:537 (1995)	
	CR	Herskowitz, "Functional Inactivation of Genes by Dominant Negative Mutations", <u>Nature</u> 329(6136):219-222 (1987)	
	CS	Holzmayr et al, "Isolation of Dominant Negative Mutants and Inhibitory Antisense RNA Sequences by Expression Selection of Random DNA Fragments", <u>Nucleic Acids Res.</u> 20(4):744-747 (1992)	
	CT	Huxley et al, "The human HPRT gene on a yeast artificial chromosome is functional when transferred to mouse cells by cell fusion". <u>Genomics</u> 9:742-750 (1991)	
	CU	Iyer et al, <u>J. Org. Chem.</u> 55:4693-4699 (1990)	
	CV	Jakobovits et al, "Germ-line transmission and expression of a human-derived yeast artificial chromosome", <u>Nature</u> 362:255-261 (1993)	
	CW	Lamb et al, "Introduction and expression of the 400 kilobase precursor amyloid protein gene in transgenic mice", <u>Nature Genetics</u> 5:22-29 (1993)	
	CX	Lavitrano et al, "Sperm cells as vectors for introducing foreign DNA into eggs: genetic transformation of mice", <u>Cell</u> 57:717-723 (1989)	

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# **INFORMATION DISCLOSURE STATEMENT BY APPLICANT**

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Sheet 5

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Group Art Unit	1635
Examiner Name	
Attorney Docket Number	EINAT=1.1D

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	CY	Lefebvre-d'Hellencourt et al, "Immunomodulation by cytokine antisense oligonucleotides" <u>Eur. Cytokine Netw.</u> 6:7 (1995)	
	CZ	Lev-Lehman et al, "Antisense Oligomers <i>in vitro</i> and <i>in vivo</i> ", in <u>Antisense Therapeutics</u> , Cohen et al, ed., Plenum Press (New York, 1997)s	
	DA	Lo, <u>Mol. Cell. Biol.</u> 3:1803-1814 (1983)	
	DB	Loke et al, "Characterization of oligonucleotide transport into living cells", <u>Proc. Natl. Acad. Sci. USA</u> 86:3474 (1989)	
	DC	Mansour, "Gene targeting in murine embryonic stem cells: Introduction of specific alterations into the mammalian genome", <u>GATA</u> 7(8):219-227 (1999)	
	DD	Morrison, "Suppression of basic fibroblast growth factor expression by antisense oligonucleotides inhibits the growth of transformed human astrocytes", <u>J. Biol. Chem.</u> 266:728 (1991)	
	DE	Niinaka et al, "Expression and secretion of neuroleukin/phosphohexose isomerase/maturation factor as autocrine motility factor by tumor cells", <u>Cancer Res.</u> 58(42):2667-2674 (1998)	
	DF	Pearson et al, "Expression of the human $\beta$ -amyloid precursor protein gene from a yeast artificial chromosome in transgenic mice", <u>Proc. Natl. Acad. Sci. USA</u> 90:10578-10582 (1993)	
	DG	Rosolen et al, "Antisense inhibition of single copy N-myc expression results in decreased cell growth without reduction of c-myc protein in a neuroepithelioma cell line", <u>Cancer Res.</u> 50:6316-6322 (1990)	
	DH	Rothstein, "Targeting, disruption, replacement, and allele rescue: integrative DNA transformation in yeast", in <u>Methods in Enzymology</u> , Vol. 194, "Guide to Yeast Genetics and Molecular Biology", Guthrie et al, eds., Academic Press, Inc. (1991), Chapt. 19, pp. 281-301	
	DI	Scanlon et al, "Oligonucleotides-mediated modulation of mammalian gene expression", <u>FASEB J.</u> 9:1288 (1995)	
	DJ	Schedl et al, "A yeast artificial chromosome covering the tyrosinase gene confers copy number-dependent expression in transgenic mice", <u>Nature</u> 362:258-261 (1993)	

Examiner Signature



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# INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet 6

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Application Number

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On Even Date Herewith

First Named Inventor

Paz EINAT

Group Art Unit

1635

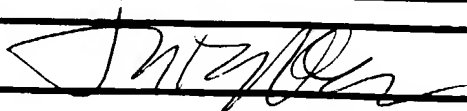
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EINAT=1.1D

## OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS

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	DK	Shaw et al, "Modified deoxynucleotides stable to exonuclease degradation in serum", <u>Nucleic Acids Res.</u> 19:747-750 (1991)	
	DL	Spitzer et al, "Inhibition of deoxynucleases by phosphorothioate groups in oligodeoxyribonucleotides", <u>Nucleic Acids Res.</u> 18:11691-11704 (1988)	
	DM	Strauss et al, "Germ line transmission of a yeast artificial chromosome spanning the murine alpha 1(I) collagen locus", <u>Science</u> 259:1904-1907 (1993)	
	DN	Thompson et al, "Germ line transmission and expression of a corrected HPRT gene produced by gene targeting in embryonic stem cells", <u>Cell</u> 56:313-321 (1989)	
	DO	Uhlmann et al, "Antisense Oligonucleotides: A New Therapeutic Principle", <u>Chem. Rev.</u> 90(4):543-584 (1990)	
	DP	Van der Putten et al, "Efficient insertion of genes into the mouse germ line via retroviral vectors", <u>Proc Natl Acad Sci U.S.A.</u> 82(48):6148-6152 (1985)	
	DQ	Wagner et al, "Potent and selective inhibition of gene expression by an antisense heptanucleotide", <u>Nature Biotechnology</u> 14:840-844 (1996)	
	DR	Wagner, "Gene inhibition using antisense oligodeoxynucleotides" <u>Nature</u> 372:333 (1994)	
	DS	Watanabe et al, "Tumor cell autocrine motility factor is the neuroleukin/phosphohexose isomerase polypeptide", <u>Cancer Res.</u> 56(13):2960-2963 (1996)	
	DT	Whitesell et al, "Episome-generated N-myc antisense RNA restricts the differentiation potential of primitive neuroectodermal cell lines", <u>Mol. Cell. Biol.</u> 11:1360 (1991)	
	DU	Wright et al, "Antisense Molecules and Their Potential for the Treatment of Cancer and AIDs", <u>Cancer J.</u> 8:185-189 (1995)	
	DV	Woolf et al, "The stability, toxicity and effectiveness of unmodified and phosphorothioate antisense oligodeoxynucleotides in <i>Xenopus</i> oocytes and embryos", <u>Nucleic Acids Res.</u> 18:1763-1769 (1989)	

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Sheet

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**First Named Inventor**

Paz EINAT

### Group Art Unit

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**Examiner Name**

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T<sup>2</sup>

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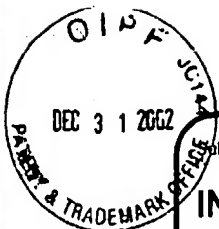
Yakubov et al, "Mechanism of oligonucleotide uptake by cells: involvement of specific receptors?", *Proc Natl Acad Sci U S A* 86(17):6454-6458 (1989)

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		Filing Date	March 6, 2002
		First Named Inventor	Paz EINAT
		Group Art Unit	
		Examiner Name	
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		Office <sup>3</sup>	Number	Kind Code <sup>5</sup> (if known)				
SPH	DU	WO	96/39426	A1	Johns Hopkins University School of Medicine	12-12-96		

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SPH	DY	KATO et al, "Expression of the Vascular Endothelial Growth Factor (VEGF) Receptor Gene, <i>KDR</i> , in Hematopoietic Cells and Inhibitory Effect of VEGF on Apoptotic Cell Death Caused by Ionizing Radiation", <i>Cancer Res</i> 55:5687-5692 (1995)	
	DW	NOMURA et al, "Possible Participation of Autocrine and Paracrine Vascular Endothelial Growth Factors in Hypoxia-induced Proliferation of Endothelial Cells and Pericytes", <i>J Biol Chem</i> 270(47):28316-28324 (1995)	
	DX	O'ROURKE et al, "Identification of hypoxically inducible mRNAs in HeLa cells using differential-display PCR Role of hypoxia-inducible factor-1", <i>Eur. J. Biochem</i> 241:403-410 (1996)	
	DY	SOKER et al, "Inhibition of Vascular Endothelial Growth Factor (VEF)-induced Endothelial Cell Proliferation by a Peptide Corresponding to the Exon 7-Encoded Domain of VEGF <sub>165</sub> " <i>J Biol Chem</i> 272(50):31582-31588 (1997)	

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